REMARKS

Claims 1-14, 16, 59 and 63-68 are pending. Claims 15, 17-58 and 60-62 have been canceled without prejudice. Claims 1, 59, 64 and 65 are amended in this response. Support for the amendments is found throughout the specification. Reconsideration of the rejection is respectfully requested.

The specification has been amended to correct a minor typographical error.

Claims 63 and 65-68 were rejected under 35 USC 112, first paragraph as containing subject matter not described in the specification. Specifically claim 63 is considered to contain NEW MATTER because using a mixture of samples from plural humans is allegedly not disclosed. Claim 65 is considered to contain NEW MATTER because "unrelated" sequences are allegedly not taught to be contained in the database. Claim 66 is considered to contain NEW MATTER because "not suspected of containing a specific infectious particle" is allegedly not disclosed. Claim 67 is considered to contain NEW MATTER because the disclosure allegedly does not disclose sequencing "at least part of a non-coding sequence". Claim 68 is considered to contain NEW MATTER because the disclosure allegedly does not disclose, "immobilized oligonucleotide microarray". This rejection is respectfully traversed.

Regarding claim 63, there are a large number of teachings in the specification to use pooled samples from multiple humans. For example, page 14, last paragraph and the first half of page 15 and the first two paragraphs on page 24. Regarding claim 65 the detection of many unrelated infectious particles simultaneously by comparison to a database of many unrelated infectious particles is taught in several locations, for example, page 12, first full paragraph and page 36 lines 2-10. As for claim 66 where the samples were not suspected of containing a specific infectious particle, note the use for sterility testing and screening of healthy samples. For example, page 7, last 5 lines, page 15, first full paragraph, page 25, last paragraph and page 29, third and fourth paragraphs. As for claim 68, the examiner notes disclosure of the same concept of a DNA microarray rather than an oligonucleotide microarray being disclosed. This dubious alleged distinction does not matter because the "oligonucleotide" wording variation for the array is disclosed elsewhere, such as page 11,

lines 19-23, page 17, lines 3-4 and other locations. Accordingly, all of the claims are supported by the specification as filed and the rejection should be withdrawn.

Claims 1-14, 16, 59, and 63-68 were rejected under 35 USC 112, second paragraph as being indefinite by the language in claim 1. Claim 1 has been reworded in a manner that avoids the potential misinterpretations noted by the examiner. The most important feature of the claim is to determine the identity of the infectious particles by sequencing directly or indirectly. Accordingly, the rejection should be withdrawn.

Claims 1, 3, 4, 6, 7, 9, 10, 12, 13, 59, 63 and 64 were rejected under 35 USC 102(b) and (e)(2) as being clearly anticipated by Reyes et al. The examiner has previously urged that Reyes et al purifies viral particles, extracts the nucleic acids, clones and sequences nucleic acids and uses probes with these sequences to assay for the virus. This rejection is respectfully traversed.

The dispute appears to be based on the term "**plurality** of infectious particles". The examiner is interpreting this to mean more than one of the same virus, all copies of each other. The reasonable conclusion is that since the sample is from a cell culture, there are thousands of PT NANB virus copies present.

The claims have been amended to prevent one from interpreting the claims in that manner. As stated throughout the specification and previously argued, this is not the present invention. The present invention is simultaneously isolating and identifying plural different types of infectious particles from the same sample. These infectious particles may be very unrelated viruses from completely different families. The claim amendment to a sample containing a plurality of different types of infectious particles avoids anticipation by a sample containing many copies of the same virus. Simply, "different types" is not "same virus". Also, claim 1 has been amended to require that the nucleic acids purified and at least partially sequenced are from at least two different types of viruses, a step not performed or suggested by Reyes et al. Note that claim 1 also requires the identification of a plurality of different types of infectious particles, a concept not even contemplated by Reyes et al.

Applicants have used the term different types of infectious particles in the specification to denote different types of viruses and the like, not multiple copies of the same virus. See the specification on page 4, lines 24-31 and page 11, lines 15-18. Page 12, lines 5-7 discusses using samples with plural "radically different classes" of infectious particles and page 13, 4th paragraph describes typical biological samples as including human infecting viruses and bacteriophages, completely different types of infectious particles. Still further, page 32, last paragraph discusses a DNA virus versus an RNA virus as a different "type" and a single stranded versus a double stranded virus as a different "type". Clearly, the present invention is much more than merely identifying one virus with a sample containing multiple copies of that virus as is taught and used by Reyes et al. The other comments made in the response filed February 6, 2004 still apply also.

Simultaneous detection of infectious particles is also performed in the present invention. The examiner has argued that detecting one virus by "simultaneously" detecting a multitude of identical virus copies is performed by Reyes et al and anticipates the present invention. Applicants note the situation in column 15, lines 33-34 mentioning a composition with 10^6 chimpanzee infectious doses of virus; hence at least 10^6 infectious particles. However, this is different from the present invention as presently claimed. By "simultaneous" applicants refer to detecting plural different types of infectious particles from the same sample. At no place in Reyes et al are multiple different viruses detected in the same sample. The claim language of the sample containing plural types and plural types of nucleic acids are sequenced and plural types are identified make it clear that applicants are not claiming identifying only one virus by the present method.

The examiner also contends that the initial sample from an individual contains a multitude of particles, some of which may be different. In theory, an individual may have multiple infections, but that is not what Reyes et al teaches. Reyes et al obtains a PT NANB virus from patients apparently infected with the one disease. There was no reason given to believe that plural different types of viruses were present. All five sequences in Figures 1-5 are obviously partial sequences because the sequence is too short to encode a virus and because the coding regions lack coding for a N-terminal methionine and because there are no regulatory sequences to promote transcription and because they were generated using

random primers annealing at various locations throughout the one virus and because Reyes et al column 3 line 45 indicates these are not complete. Even a small virus can easily contain all of the sequences shown in Reyes et al with plenty of room to spare.

Throughout the Reyes et al reference, the wording presumes only one virus is being detected. Even the passage cited in the office action as hinting at plural virus types does not teach plural viruses. On page 8, lines 14-16 of the office action state "the Reyes et al disclosure is not limited to one infectious particle type because Figures 1-5 as previously cited in the bridging sentence between columns 2 and 3 disclose from different sequence containing virus specimens". This assertion is contrary to the teaching of the bridging sentence and many other teachings in Reyes et al. The bridging sentence is:

> "The virus may be further characterized as having a genome comprising RNA sequences which may be reverse transcribed to obtain at least one of the c DNA sequences shown in FIGS. 1-5."

The sentence clearly states "the virus" in the singular form. The sentence clearly states that "the virus" (singular) has "a genome" in the singular form. The sentence also states "a genome comprising RNA sequences...FIGS. 1-5" (plural form). The sequences of FIGS. 1-5 are partial sequences, which together are part of "a genome" (singular form) of "the virus" (singular form). At no point are multiple different viruses taught. This interpretation is further supported in the same paragraph in column 3 lines 8-9 which state "These sequences are derived from different segments of the viral genome".

Further, the sequences were determined to be from the virus by screening with antisera from PT NANB patients. See column 15, lines 8-11. The intention is to find one virus. The probability that the patient providing the PT NANB sample and the patients providing the antisera being infected with the same PT NANB virus is reasonable but it is unlikely for these two groups of patient(s) to each be infected with a second unrelated virus.

The last two lines on page 6 of the office action mailed May 4, 2004 state that "...five different viruses were identified in Figures 1-5...". From the above discussion it should be clear that this is an improper interpretation of Reyes et al and requires an assumption contrary to Reyes et al.

Furthermore, the examiner's assertion in the first 2 lines on page 7 of the office action is that "within a single PT NANBV specie of virus, are reasonably interpreted as differing infectious particles". Even if a mutation or some variation could theoretically exist (an unsupported speculation), Reyes et al teach diagnosing one disease by identifying one virus. Reyes et al do not teach identifying multiple viruses as the present claims require "determining the identity of the plurality of different types of infectious particles" (claim 1 last clause). Also, Reyes et al indicate their partial sequences are from the same virus and do not suggest sequencing two or more nucleic acids from two or more different types of viruses.

Therefore, the rejection is improper, particularly for the presently amended claims, and should be withdrawn. Furthermore, the rejection is incomplete because it has not shown where or how Reyes et al mentions or suggests many of the features found in many of the dependant claims.

For example, claim 2 recites that the biological sample is pooled from multiple individuals. This feature is not taught and Reyes et al suggests otherwise by always using samples from only one individual at a time. See column 9, lines 46-49 describing the general method as starting with "plasma from a human or ... a chimpanzee..." This is repeated in Example 2 first sentence where "a chimpanzee" is inoculated with a sample from "a patient". Likewise in Example 4 where the virus from "human plasma from an individual" was passaged from "a chimpanzee" to "a second chimpanzee". The use of only one sample is dramatically shown in Table 2 where 8 assays were done, each one using a sample from only one individual. Since pooling biological samples is never done but rather the opposite was performed several times, Reyes et al does not teach pooling but rather motivates one to do the opposite.

Claims 5 and 6 require detecting two infectious particles, an old and a new or two new infectious particles. Reyes et al does not mention ever finding a known virus. Reyes et al think they have found one new virus and present no suggestion that two new ones were found. Further, Reyes et al does not find two or more viruses simultaneously.

Claims 10 and 64 recite isolating infectious particles based on sedimentation coefficient ranges and use density gradients to purify particles from primary biological

samples. Reyes et al never separates based on sedimentation values. The centrifugation steps taught by the reference either lack any gradient (sample pelleted in Examples 1+) or are centrifuged to equilibrium to a given density (18 hours in Examples 2+). Furthermore, the density gradients used by Reyes et al are only used for isolating viruses from previously cultured viruses, not primary biological samples such as serum from a patient where the virus is not cultured. This difference may be important because primary biological samples are more complex and the virus may be bound to antibodies and other material.

Claim 14 requires at least two nucleic acid sequences to be overlapping in order to perform the claimed method. None of the sequences in Reyes et al appear to overlap. Therefore, Reyes et al cannot reasonably anticipate the claimed method.

Claim 16 qualifies the sample being tested as being a product for use, such as a food or pharmaceutical, not a clinical sample. None of the samples being tested in Reyes et al are potential products for use and Reyes et al does not suggest such a purpose for their invention.

Claim 63 recites using mixed samples that are pooled from multiple humans. Note that this claim is dependant on claim 2. Reyes et al never mixes samples together for assaying. Note the locations noted above where each sample is from an individual, not a pooled sample. Also note column 7, lines 21-25 and column 8, line 44 as suggesting the use of a homogenous sample, not a mixed sample from more than one individual.

Claim 65 requires the database to contain sequences from different families of infectious particles as well as the different types of infectious particles recited in the base claim. The examiner has argued that the term database has no minimum size and thus comparison of the sequences in Reyes et al to other hepatitis viruses constitutes a database comparison. Newly amended claim 65 requires a minimum content of database containing sequences from different families of infectious particles, something not used by Reyes et al.

Claim 66 recite that the samples "are not suspected of containing a specific infectious particle". This is completely opposite from Reyes et al where the virus originated from samples from patients with PT NANB disease.

Claim 67 recites determining at least part of the non-coding sequence of the infectious particle. This is quite different from Reyes et al which reports only coding

sequences (e.g. FIG. 1) and can only find coding sequences because the clones are selected for using antisera against viral proteins (column 15, lines 8-11, and to a lesser extent column 16, lines 45+ and column 17, lines 64+). Still further Reyes et al obtains their clones by reverse transcribing RNA. Most RNA is from the coding sequence. Note that the sequences in Reyes et al do not even include a trivial non-coding sequence such as a stop codon, a poly A tail or tRNA.

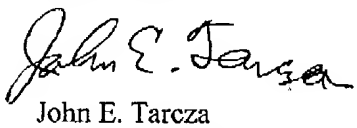
Claim 68 recites using a microarray for nucleic acid identification. Nothing in Reyes et al suggests this claim.

CONCLUSIONS

In view of the amendments and comments above, the rejections have been overcome. Reconsideration, withdrawal of the rejections and early indication of allowance are respectfully requested. If any issues remain, particularly details of the claim language, the examiner is encouraged to telephone the undersigned.

If needed, applicants petition for an extension of time under the provisions of 37 CFR 1.136(a) for sufficient time to accept this response. The commissioner hereby is authorized to charge payment of any fees under 37 CFR § 1.17, which may become due in connection with the instant application or credit any overpayment to Deposit Account No.500933.

Respectfully submitted,



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